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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,271	06/22/2001	Timothy G. Myers	41570	6793

7590 03/18/2004

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,271	MYERS ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *13-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-12) is acknowledged.

Applicant further elected species MSN 28 from the table corresponding to a marker for

Diabetes telephonically on March 12, 2004.

2. The traversal is on the grounds that Group II should be examined with Group I, as the claims are dependant on the claims of Group I and should not have a burden. Applicant admits that there is a difference between Group I and III, however, concludes that they should be examined together. This argument is not persuasive. With regard to the argument of dependency, this is not a factor in restriction practice. The MPEP in Chapter 800 state that restriction requirement is proper if the invention is independent and distinct. Group I encompasses a method and Group II has a product, which can be used in a different process. Furthermore, Group I does not have a generic linking claim such as a genus which would include the species or dependent claims of Group II. Applicant also contends that Group III should be rejoined to Group I, which is directed to a method of monitoring efficacy of a therapy for a disease. Clearly this method is separate from Group I, which has a different end result. The search of the above groups is not coextensive; a reference that would anticipate or render obvious one invention would not anticipate or render obvious the other Groups. However, if applicant is willing to make a statement on the record that a single reference would anticipate or render obvious all three Groups they will be examined together. Further burden is established as each Group has acquired a separate status in the art. Therefore,

applicant's comments are not persuasive. Applicant's statements have been considered and addressed, the restriction requirement is deemed proper and is final.

Claim Disposition

3. Claims 1-55 are pending. Claims 1-12 are under examination.

Claim Objection

4. Claims 7 and 8 are objected to for the recitation of " p<0.01 and p<0.001". The correct phrase is "at p<0.01", for example.

Correction is required.

Specification

5. The specification is objected to because of the following informalities:

The specification is objected to because on page 3 following the citations there appears the statement "not prior art". In addition, the specification is objected to for the incorporation of essential material into the specification, see Tables 1-5 on pages 15-17. The tables list Accession numbers, however, there is no indication of the source of the information provided. Chapter 600 of the MPEP state that the referencing application should include an identification of the referenced patent, application or publication. Particular attention should be directed to specific portions of the referenced document

where the subject matter being incorporated may be found. Therefore, the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Correction is required.

Oath/Declaration

6. The Oath/Declaration is objected to because it does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Title

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed. The title is directed

to "non-genetic protein disease markers" whereas the elected invention is directed to a "method for determining a disease state".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for protein markers and a method of determining the disease states using said markers for obesity, osteoporosis, diabetes, osteoarthritis and hypertension, does not reasonably provide enablement for any or all disease states for any or all diseases (see for example claims 1, 5-8 and 10). The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Factors considered in determining whether undue experimentation is required, are summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Circ. 1988). They include but are not limited to: quantity of experimentation, the amount of direction or guidance presented, the presence or absence of working example, the nature of the invention, the state of the prior art, the relative skill of those in the art, predictability or unpredictability of the art and breath of the claims. The factors will be discussed below.

The claims are directed to a method for determining a disease state of a subject (see for example claim 1). The specification and dependent claims recite that the diseases are obesity, osteoporosis, diabetes, osteoarthritis and hypertension as set

forth in Tables 1-5 (see pages 15-17 of the instant specification). However, the claims broadly recite "a disease state of a subject" and there is no indicia for example in claim 1 as to what disease. Note that the Tables on pages 15-17 disclose five different diseases with no overlapping markers, which demonstrates that a marker is specific to a disease. The specification does not describe/provide examples to demonstrate that the markers identified in the tables are applicable for all possible diseases or any showing all possible protein markers. In fact on page 8 of the specification it is stated that "some protein markers may be disease-specific". Furthermore, the breath of the claims encompass genetic and non-genetic variation, which is not enabled by the instant specification. The specification on page 5 disclose that the invention determined non-genetic markers by searching for proteins present in abnormal abundances between monozygotic twins where the twins are discordant for the disease state".

Additionally, the method as set forth in claim 1 provides the steps of: (a) obtaining a biological sample containing protein, (b) measuring levels of protein markers of the disease state and (c) comparing the levels of said markers to a standard. These steps alone cannot achieve the claimed objective in the preamble. On page 5 of the instant specification it is stated that "initially all readily detectable proteins are measured, but after the markers are determined, an assay for the markers alone is sufficient. Clearly the method is missing essential steps between the obtaining a sample and measuring levels of protein markers such as an identification step for the markers. Thus, one of skill in the art would have to engage in undue experimentation to determine what other diseases, if any, the identified markers can be applied to or identify other markers associated with the unspecified amounts of diseases encompassed by the claims. Due to the large quantity of experimentation necessary to generate the protein markers for all possible disease states, based on the infinite

number of disease states and markers recited in the claims, and due to the lack of adequate guidance/direction provided in the instant specification, this is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

The specification does not provide clear guidance as to the proteome of the claimed invention to allow one of skill in the art to practice the claimed invention commensurate in scope with the claims. For example , claim 6 recites "measuring levels of individual proteins in a proteome" and the specification on page 5 refers to the proteome as a signature or proteomic pattern created by protein markers. It is also disclosed that the proteome is a large number of proteins expressed in a biological sample, representing the total, relevant portion or preferably all detectable proteins by a particular technique or combination of techniques. Clearly, the description provided is inconsistent and confusing, whereas, the prior art states that "the image of the displayed proteins obtained is the proteome" (see Page et al., Research Focus, vol. 4, no. 2, February 1999). Additional, the tables listed on pages 15-17 (and recited in for example, claim 2) provides a listing of protein markers labeled with Accession numbers, however, the specification does not provide adequate guidance as to the source of the accession numbers to make the information readily accessible and to be enabling. Therefore, one of skill in that art would have to engage in significant experimentation to practice the claimed invention in a manner that reasonable correlate with the invention as claimed.

In view of the foregoing, one of skill in the art would require guidance, beyond that provided in the instant specification, in order to practice the claimed invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and the dependent claims hereto are indefinite for the recitation of "a biological sample containing protein from said subject", because the term "protein" is confusing as it is not clear which protein is being referred to; said biological sample contains thousands of proteins. The skilled artisan would not know which particular protein to manipulate.

Claim 2 represents an improper Markush, because the Markush group is not recited in the claim, it refers to tables in the specification, therefore is incomplete.

Claim 3 lacks proper antecedent basis as claim 2 does not recite the protein markers, the claim merely refers to tables in the specification. It is suggested that claim 2 is amended to recite the specific markers as the limitations of the specification cannot be read into the claims.

Claim 6 recites "proteins are increased or decreased" which is confusing as it is unclear whether this means and increase/decrease in the content of particular proteins in the gel or an increase/decrease of size/molecular weight of said proteins. The claim is also confusing for the recitation of "levels of individual proteins in a proteome", as a particular protein in a particular proteome of a particular biological sample can only have one level. How can multiple levels be determined and compared? See also page 5 of

the specification where it is stated that "proteome" is equivalent to a "signature". The dependent claims hereto are also included.

Claim 8 is incomplete because the claim is missing a transitional phrase where the claim recites "the method of claim 7 wherein $p<0.001$".

Claims 11 and 12 are indefinite as the claims are substantial duplicates, claim 11 recites "tables 1-5" and claim 12 recites the names of the diseases which are reported in the tables.

Claim 12 is confusing where the claim recites " a protein marker of claim 11 selected from the proteins are markers". It is suggested that the claim be rewritten as "a protein marker of claim 11, wherein said marker is for the diseases selected from the group consisting of...".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3, 4, 6, 9 and 10 are rejected under 35 U.S.C 102(b) as being anticipated by Pleibner et al. (Electrophoresis, vol. 19, pages 2043-2050,1998).

Pleibner et al. teach a method that uses protein markers to identify alterations of the cardiac protein pattern in renovascular hypertension, which provides useful information regarding the disease state (claim 1). For instance, the method of Pleibner et al. detected a protein that is likely to be in the same pathway of the disease stage, for example, early stage of hypertension (claim 5, see page 2049 of the reference). Pleibner et al. used a group of hypertensive (claims 3, 4 and 9) and control rats and compared the patterns by computer assisted two-dimensional (2-D) gel electrophoresis (claim 10) and analysis including univariate and multivariate statistical approaches (see pages 2043-2044). Total proteins, for example, proteome (claim 6) of tissue samples are separated and the level of individual protein separated is measured through 2-D gel analysis assisted with computer analysis (see page 2044, left column). Thus, the limitations of the claims are met by this reference.

Conclusion

11. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner

ROBERT A. WAX
PRIMARY EXAMINER